

## **Abstract**

### **Background**

Histopathology is often essential in medicine to establish an accurate diagnosis, which forms the basis of disease treatment. Pathology laboratories are scarce in most Sub-Saharan Africa (SSA) where Dermatopathology is only a developing field. In resource-poor countries, most specimens are analysed only after Haematoxylin and Eosin staining (H&E). The availability of other special stains (SS) is very limited and restricted to only few centres. The aim of this study is to analyse the extent of dermatopathological cases which can be adequately diagnosed after H&E alone. Secondly, to investigate which cases required further SS.

### **Methods**

All skin specimens submitted to two University Hospitals (Tanzania and Kenya) were included in this study. All specimens were first analysed with H&E and a diagnosis established when possible. All cases in which an accurate diagnosis after H&E only was not possible, were registered and evaluated after further SS.

### **Results**

A total of 386 specimens were examined. A proper histological diagnosis with H&E alone was possible in 344 (89.1%) samples. In 45 (11.6%) cases, mostly skin infections, further SS were necessary.

### **Conclusion**

A proper histological diagnosis was possible after H&E alone in almost 90% of the specimens submitted to the two laboratories in SSA.

### **Key Words**

Dermatopathology, Sub-Saharan Africa, special stains, laboratories, developing countries

## Introduction

Histopathological analyses and clinical-pathological correlation are often essential to establish an accurate diagnosis of skin diseases. Nevertheless, pathology/dermatopathology services are not yet routinely used in the diagnostic procedures by a dermatologist working in Sub-Saharan Africa (SSA) where the majority of skin diseases are diagnosed clinically without the utilization of any other diagnostic procedure<sup>1</sup>.

In developing countries, histopathological diagnosis is still frequently hampered by the scarce availability of histology laboratories, poorly developed infrastructure, poor quality of specimens and shortage of well-trained and experienced pathologists<sup>2,3,4,5</sup>. Frequent diagnostic delays and misdiagnoses are also factors influencing the decision whether a skin biopsy is necessary. Moreover, the decision to take a skin biopsy also depends on the suspected clinical diagnosis, the experience of the clinician, the economic situation of the patient, the availability of a pathology laboratory and the availability of a pathologist/dermatopathologist<sup>6</sup>.

Haematoxylin and Eosin staining (H&E) is routinely used worldwide for examining the majority of histological specimens including skin biopsies. Other histochemical stains ("special stains - SS") such as periodic acid-Schiff (PAS), Gram, Ziehl-Neelsen (ZN), mucin, and Giemsa are routinely used when particular tissue characteristics cannot be identified after H&E alone. Although SS are cheap and easy to prepare, their utilization is scarcely reported in SSA<sup>7</sup>, probably because such stains are only available in a few centres<sup>8</sup>.

Immunohistochemistry and immunofluorescence are available only in very few University Hospitals and in some private laboratories in SSA.

Dermatopathology is an emerging field of medicine limited to a few countries in SSA<sup>2,8</sup> where there are no dermatopathology fellowships at all. Trying to fill this gap we have been running a project to develop dermatopathology supported by the European Academy of Dermatology and Venereology (EADV) for the last four years. The aim is to develop dermatopathology in SSA by offering dermatopathology training to young and motivated African dermatologists/pathologists who are interested in dermatopathology.

As a part of this project, we are interested to study the number of skin specimens that can be evaluated accurately after H&E alone in routine cases from SSA. This study shows the importance of SS in SSA and helps to understand the costs of providing pathology/dermatopathology services in poor resource settings.

## Materials and Methods

A prospective observational study was done between January and December 2013. All skin biopsies received for analysis at the Regional Dermatology Training Center (RDTC), Moshi Tanzania and the County Teaching and Referral Hospital (CTRH), Kakamega, Kenya were included. All samples were registered consecutively, and none was excluded. The laboratories at these hospitals received skin biopsies or excisions from dermatologists, dermato-venereology officers and general practitioners.

Formalin 10% was used in fixing all samples. The samples were embedded in paraffin and routinely processed. All slides were stained with H&E and evaluated by a board-certified dermatopathologist (KS) (ICDP – UEMS International Board Certification in Dermatopathology, Frankfurt, Germany) in conjunction with the clinical information mentioned on the request form. Additional SS (Periodic acid-Schiff (PAS), Gram, Ziehl-Neelsen (ZN), colloidal iron and Giemsa) were performed if a correct diagnosis was not possible after H&E alone. In some cases, deeper cuts were necessary. Other SS, immunohistochemistry and immunofluorescence techniques were not available at these two centres. Nevertheless, all instances that required the use of further techniques for establishing a correct diagnosis were registered. In six cases the biopsies were sent to a reference centre in Europe for immunohistochemical evaluation.

A specific diagnosis was made when possible. If not possible, the cases were classified according to the following reaction patterns: A) Inflammatory: Inflammatory not otherwise specified (n.o.s.), spongiotic, psoriasiform, lichenoid, bullous, vasculopathic, panniculitis, granulomatous. B) Tumours: malignant tumours, benign tumours. C) Infections: Infection n.o.s., viral, bacterial, fungal, and protozoan. D) Other.

This study was ethically cleared by Kakamega Hospital Research and Ethics Committee and permission for research was obtained from RDTC. Statistical analyses were done with SPSS version 16 (IBM SPSS Statistics).

## Results

We examined a total of 386 skin biopsies. The median age of the patients was 39 years with a Male to Female ratio 1:1. The most frequent diagnoses were squamous cell carcinoma (SCC), Kaposi's sarcoma (KS), lichen planus, and psoriasis vulgaris (Table 1). Inflammatory conditions (51%) and tumours (38.3%) represent the vast majority of the cases (Table 2).

A proper diagnosis was possible after H&E alone in 344 (89.1%) skin biopsies. Deeper cuts were performed in 53 (13.7%) specimens. SS were necessary in 45 (11.6%) cases (Table 3).

The most frequent diagnoses using SS were dermatomycosis (n=8) and leprosy (n=4) (Table 4).

Immunohistochemistry (n=13) and immunofluorescence (n=7) analyses would have been necessary for the correct diagnosis of 20 cases.

## **Discussion**

The aim of the study is, to identify the amount of correct histological diagnosis of dermatopathology specimens after H&E alone, and to understand the importance of SS to establishing the accurate diagnosis in a SSA-setting.

The majority of the histological diagnoses were inflammatory conditions (51%), followed by tumours (38.3%) and infectious conditions (7.8%) (Tables 1 and 2). Similar data were published in other dermatopathological studies from SSA<sup>7,9</sup>. Clinical studies from SSA reported higher skin infections (50-85%)<sup>10,11</sup> suggesting that infectious skin diseases were not often biopsied.

In our study, the majority (89.1%) of the specimens were analysed after H&E alone, nevertheless in 13.7% of cases deeper cuts were necessary. The rate of deeper sections reported in the dermatopathology literature has varied from 7% to 37.3% of cases<sup>12</sup>. There are several reasons for the necessity of deeper cuts such as sampling error during macroscopy, small biopsy, unspecific findings, financial reasons, time constraints, and inexperienced laboratory staff or poor quality of laboratory facilities<sup>6,12</sup>. In this study, as in many other laboratories in SSA, the necessity for deeper cuts was due to the poor quality of the original slides. It is frequently a direct consequence of insufficiently trained laboratory personnel and poor quality of laboratory facilities and materials. These are well known and common problems in laboratories in developing countries.

Considering the most frequent specific diagnoses (Table 1) and histological patterns (Table 2), which shows several tumours and few infections, one can imagine that most of the diagnoses can be established after H&E alone. In 11.6% of cases where SS were necessary (Table 4), we found frequently infections (86.3%), mostly dermatomycoses, leprosy, and tuberculosis. Maingi et al.<sup>6</sup> reported similar findings where most of the SS were necessary to diagnose an infection.

Immunohistochemistry and immunofluorescence would have been necessary for a correct diagnosis in 3.3% and 1.8% respectively, of all specimens. Most of the cases requiring immunohistochemical stains were tumours, whereas most of the cases requiring immunofluorescence analyses were inflammatory blistering disorders.

We are conscious of the following limitations of our study: small number of samples, only two specialised centres in East Africa. This study was conducted at two tertiary institutions with developed dermatology and pathology/dermatopathology services and therefore, cannot be generalized to all health facilities in East Africa.

## **Conclusion**

A correct histological diagnosis was possible in the majority (up to 90%) of specimens after H&E only. In about 10% of the cases, further SS were needed, mostly PAS to establish or confirm the diagnosis of cutaneous infections. Since SS are affordable in SSA, they should be introduced to all pathology laboratories. Deeper cuts are often necessary because of poor quality slides. Therefore, there is need to improve the quality of training of the laboratory personnel and the quality of processing the specimens. There is also need to introduce immunohistochemistry and immunofluorescence analyses to improve the diagnostic accuracy of tumours and autoimmune bullous diseases. We believe that these more costly techniques should be available at least in one large public (University-) Hospital in each country. The current small number of cases do not justify the introduction of these expensive procedures in all pathology units.

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## **References**

1. Hoenecke H, Lee V, Roy I. Pathologists Overseas. Coordinating volunteer pathology services for 19 years. Arch Pathol Lab Med 2011;135:173-178.
2. Tsang MW, Kovarik GL. Global access to dermatopathology services: physician survey to availability and needs in sub-Saharan Africa. J Am Acad Dermatol 2010;63:346-348.
3. Berezowska S, Tomoka T, Kamiza S, Milner DA, Langner R. Surgical pathology in sub-Saharan Africa-volunteering in Malawi. Virchows Arch 2012;460:363-370.
4. Adeyi OA. Pathology Services in Developing Countries-The West African Experience. Arch Pathol Lab Med 2011;135:183-186.

5. Kaschula ROC. The practice of pathology in Africa. *Arch Pathol Lab Med* 2013;137:752-755.
6. Maingi CP, Helm KF. Utility of deeper sections and special stains for dermatopathology specimens. *J Cutan Pathol* 1998; 25:171-175.
7. Gimbel DC, Legesse TB. Dermatopathology practice in Ethiopia. *Arch Pathol Lab Med* 2013;137:798-804.
8. Gimbel DC, Sohani AR, Busarla SV, et al. A static-image telepathology system for dermatopathology consultation in East Africa: The Massachusetts General Hospital Experience. *J Am Acad Dermatol* 2012; 67: 997–1007.
9. Beltraminelli H, Kiprono S, Zuriel D et al. Dermatopathology in sub-Saharan Africa: a systematic 5-years analysis of all histopathological diagnoses from the Regional Dermatology Training Centre (RDTC) in Moshi, Tanzania. *J Eur Acad Dermatol Venerol* 2014; 29:1370-5.
10. Bissek ACZK, Tabah EN, Koutou E, et al. The spectrum of skin diseases in a rural setting in Cameroon (sub-Saharan Africa). *BMC Dermatology* 2012;12:7.
11. Gibbs S. Skin disease and socioeconomic conditions in rural Africa: Tanzania. *Int J Dermatol* 1996; 35: 633–639.
12. Stuard LN, Rodriguez AS, Gardner JM et al. Utility of additional tissue sections in dermatopathology: diagnostic, clinical and financial implications. *J Cutan Pathol* 2014;41:81-87.

## Tables

Table 1: Top 11 specific histological diagnoses

Histological diagnosis	Frequency	%
Squamous cell carcinoma (SCC)	26	6.7
Kaposi's sarcoma	23	6
Lichen planus	21	5.4
Psoriasis vulgaris	15	3.9
Basal cell carcinoma (BCC)	10	2.6
Bullous pemphigoid	9	2.3
Cutaneous lymphoma	9	2.3
Pemphigus vulgaris	8	2.1
Cut. Lupus erythematosus	8	2.1
Molluscum contagiosum	8	2.1
Pityriasis rosea	8	2.1

Table 2: The distribution of all biopsies (n=386) according to histological patterns

Histological pattern	Frequency	%
Inflammatory	197	51
Spongiotic	79	20.5
Lichenoid	33	8.5
Psoriasiform	30	7.8
Vesicobullous	26	6.7
Inflammatory n.o.s.	23	6.0
Vasculopathic	6	1.6
Tumours	148	38.3
Malignant tumours	89	23.0
Benign tumours	59	15.3
Infections	30	7.8
Viral	14	3.6
Fungal	11	2.8
Bacterial	5	1.3
Other	11	2.8

Table 3: Frequency of all stains and deeper cuts

Stain	Frequency	%
Haematoxylin and Eosin only	344	89.1
Periodic acid-Schiff (PAS)	22	5.7
Gram	9	2.3
Mucin	7	1.8
Ziehl-Neelsen	6	1.6
Giemsa	1	0.3
Deeper cuts	53	13.7

Table 4: Most frequent diagnoses with special stains

Disease	Frequency
Dermatomycosis (PAS)	8
Leprosy (Z.N.)	4
Cutaneous lupus erythematosus (Mucin)	3
Pityriasis versicolor (PAS)	3
Cutaneous tuberculosis (Z.N.)	2
Cutaneous histoplasmosis (PAS)	2